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JUL 17 2007

Atty. Dkt. No. 10010381-1
USSN: 09/944,083**REMARKS**

In view of the following remarks, the Examiner is respectfully requested to withdraw the rejections and allow claims 7-26 and 44-51, the only claims pending and currently under examination in this application.

With this response, Applicants amend claims 7 and 16. Support for the amendments to the claims may be found, for example, in the specification at page 16, paragraph 63, wherein it is set forth that the subject arrays include at least two different polymer ligands that differ by monomeric sequence covalently attached to different and known locations on a substrate surface.

As no new matter is added by way of these amendments, their entry by the Examiner is respectfully requested.

Claim Rejections – 35 U.S.C. § 102

Claims 7-10, 13, 14, 16-18, 22, 23, 25, 26, 44, 48 and 49 have been rejected under 35 U.S.C. § 102(a) as allegedly anticipated in view of Barner et al. (EP 0596421 A1). The rejection is respectfully traversed for at least the following reasons.

Legal anticipation requires that a single prior art reference expressly or inherently disclose each and every limitation of a claim. While the reference must also provide an enabling disclosure of how to make and use the claimed subject matter, the initial inquiry is whether the claimed invention is described by the reference. *Dayco Products, Inc. v. Total Containment, Inc.*, 329 F.3d 1358, 1368 (Fed. Cir. 2003); *Verdegaal Bros. v. Union Oil of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). Additionally, the identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1566 (Fed. Cir. 1990).

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Here, claims 7 and 16, the only independent claims of the subject application recite:

A method of producing an array of at least two different polymer ligands that differ by monomeric sequence covalently attached to different and known locations of a surface of a substrate, said method comprising:

- (a) providing a substrate having a surface displaying olefin functional groups that consist of a single site of unsaturation by contacting said surface with a derivatizing composition comprising at least a first silane having an olefin functional group;
- (b) converting said olefin functional groups to ligand reactive functional groups that produce covalent bonds with said at least two different polymer ligands upon contact with said ligands; and
- (c) contacting said surface with said at least two different polymer ligands that differ by monomeric sequence to covalently bond said at least two different polymer ligands to different and known locations of said surface and produce said array. (Claim 16 is similar to claim 7 but specifies nucleic acids rather than polymer ligands.)

It follows that a feature of the pending claims is:

"an array of at least two different polymer ligands that differ by monomeric sequence covalently attached to different and known locations of a surface of a substrate ..." (claim 7) and "an array of at least two different nucleic acids that differ by monomeric sequence covalently attached to different and known locations of a surface of a substrate ..." (claim 16). As such, the claimed methods produce an array containing different polymer ligands or nucleic acids that differ by monomeric sequence in discrete locations on the same surface.

Applicants' specification clearly teaches this concept throughout the disclosure, such as, for example in the following paragraph:

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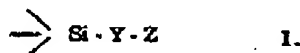
"[t]he subject arrays include at least two distinct polymers that differ by monomeric sequence covalently attached to different and known locations on the substrate surface. Each distinct polymeric sequence of the array is typically present as a composition of multiple copies of the polymer on the substrate surface, e.g. as a spot on the surface of the substrate. The number of distinct polymeric sequences, and hence spots or similar structures, present on the array may vary, but is generally at least 2, usually at least 5 and more usually at least 10, where the number of different spots on the array may be as high as 50, 100, 500, 1000, 10,000 or higher..." (Specification at page 16, ¶[63]).

The Examiner asserts that Barner teaches "a method of producing an array of at least two different polymer ligands covalently attached to [*sic:the*] surface of [*sic:a*] substrate," (Office Action dated April 17, 2007 at page 3, lines 4-5). In support of this assertion, the Examiner points to the Abstract, and the bottom of page 7 of Barner, pictured below.

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Abstract

The present invention is concerned with the coating of dielectric TiO_2 wave guides with biologically recognizing elements to give biosensors having high sensitivity and specificity for an analyte molecule. The coating consists of an organic carrier layer to which receptor molecules are bonded, the carrier layer having an ordered monomolecular layer which consists of molecules of general formula I



This layer is bonded directly to the TiO_2 wave guide via the Si atom or, if desired, is bonded to a TiO_2 wave guide via an intermediate layer. The receptor molecules are biological molecules having recognizing properties, such as antigens, antibodies, receptors, dsDNA, ssDNA. The arrangement of the receptor molecules on the sensor surface can be not only two dimensional but also three dimensional, and the receptor molecules can be immobilized non-directed or directed on the organic carrier layer.

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The Abstract, however, merely discloses that "[t]he receptor molecules are biological molecules ... such as dsDNA and ssDNA" which can be arranged on a sensor surface in either a two or three dimensional format. By this statement, Barner simply suggests that such molecules may be anchored to a planar or porous surface. Nowhere is there a description (let alone an enabling teaching) of "an array of at least two different polymer ligands of different monomeric sequence," at known locations on the same surface. In fact, the Abstract teaches that the "biosensors [have] high sensitivity and specificity for an analyte molecule." By this, the skilled artisan would understand that Barner is not describing a device of two or more ligands that differ by monomeric sequence as claimed.

Neither does the teaching referenced by the Examiner at the bottom of page 7 describe Applicants' claim element of "an array of at least two different polymer ligands [or nucleic acids] that differ by monomeric sequence." The disclosure at the bottom of page 7 is reproduced below:

carrier layer. Non-directed immobilization of a receptor molecule to the organic carrier layer signifies that in the bonding of the receptor molecule to the organic carrier layer no regard is had to particular structural features of the receptor molecule, i.e. the immobilization takes place at any position on the surface of the receptor molecule. Directed immobilization signifies that in the immobilization of the receptor molecule regard is had to the analyte-recognizing domains and for the immobilization those

In this disclosure, Barner simply states that "[n]on-directed immobilization of a receptor molecule to the organic carrier layer signifies that in the bonding of the receptor molecule to the organic carrier layer no regard is had to particular structural features of the receptor molecule, i.e., the immobilization takes place at any position on the surface of the receptor molecule." The Examiner has construed this sentence to indicate that "non-directed immobilization occurs affording many 'different' points of attachment, i.e., produces 'different'

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molecules with different 'substitutions' at the linking points," (Office Action dated April 17, 2007 at page 3, lines 6-8).

Applicants must respectfully disagree as the phrase "[a]ny position on the surface of the receptor molecule" does not signify that different molecules are attached at different positions on the surface of the substrate. Rather, this phrase means that the receptor can be attached to the substrate at different positions in the receptor, e.g., a nucleic acid may be attached at its 3' or 5' end, or somewhere in between.

Therefore, the optical biosensor of Barner is not "an array of at least two different polymer ligands [or nucleic acids] that differ by monomeric sequence covalently attached to different and known locations of a surface of a substrate" as claimed by Applicants because such a structure requires that two or more distinct polymers or nucleic acids be covalently attached to different and known locations on a solid surface. Barner fails to teach this element. Indeed, Barner repeatedly refers to the biosensor as designed to detect a singular analyte. The skilled artisan envisages only that the same ligand populates a substrate surface. (See, e.g., page 7, lines 1, 31 and 36 wherein there is reference to "a receptor/analyte," "a receptor molecule," and "the receptor molecule".

Because Barner does not teach or describe each and every element of the claimed invention, it cannot anticipate it. Accordingly, Applicants submit that the claims are novel in view of this reference and respectfully request that the rejection under 35 U.S.C. § 102(a) be withdrawn.

Claim Rejections – 35 U.S.C. § 103

Claims 7-10, 13, 14, 16-19, 22, 23, 25, 26, 44, 48-51 have been rejected under 35 U.S.C. § 103(a) as allegedly obvious over Barner et al. (EP 0596421 A1) in view of Beattie et al. (WO 95/11755) and Sanchez-Carbayo et al. (Curr.

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Org. Chem. 2000, 4:945-71). The rejection is respectfully traversed for at least the reasons set forth below.

In order to meet its burden in establishing a rejection under 35 U.S.C. § 103 the Office must first demonstrate that the combined prior art references teach or suggest all the claimed limitations. See *Pharmastem Therapeutics v. Viacell et al.*, 2007 U.S. App. LEXIS 16245 (Fed. Cir. 2007) ("the burden falls on the patent challenger to show by clear and convincing evidence that a person of ordinary skill in the art would have had reason to attempt to make [every element of] the composition or device, or carry out the [entire] claimed process, and would have had a reasonable expectation of success in doing so," (citing *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1740 (2007); and see *Omegaflex, Inc. v. Parker-Hannifin Corp.*, 2007 U.S. App. LEXIS 14308 (Fed. Cir. 2007) ("[t]he Supreme Court recently explained that 'a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art,' (citing *KSR Int'l Co.* at 1741); and see *Dystar Textilfarben GmbH v. C.H. Patrick Co.*, 464 F.3d 1356, 1360 (Fed. Cir. 2006) ("[once] all claim limitations are found in a number of prior art references, the factfinder must determine '[w]hat the prior art teaches, whether it teaches away from the claimed invention, and whether it motivates a combination of teachings from different references,' (citing *In re Fulton*, 391 F.3d 1195, 1199-1200 (Fed. Cir. 2004)))).

Here, a feature of the pending claims is "an array of at least two different polymer ligands [or nucleic acids] that differ by monomeric sequence covalently attached to different and known locations of a surface of a substrate ..."

Barner fails to teach or suggest this required element for the reasons set forth above. Therefore, Barner is deficient in teaching or suggesting all the claimed limitations. As Beatie and Sanchez-Carbayo were cited solely for their alleged disclosure of the use of cDNA in biosensors, neither reference remedies

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the deficiencies of Barner.

Because the references, either alone or when combined, fail to teach all the claim limitations, they cannot render the claimed invention obvious under 35 U.S.C. § 103(a). Accordingly, a *prima facie* case of obviousness has not been established and Applicants respectfully request that the rejection of claims 7-10, 13, 14, 16-19, 22, 23, 25, 26, 44, 48-51 be withdrawn.

Claims 7-14, 16-23, 25, 26, 44, 48-51 have been rejected under 35 U.S.C. § 103(a) as allegedly obvious over Barner et al. (EP 0596421 A1) in view of Beatie et al. (WO 95/11755) and Sanchez-Carbayo et al. (*Curr. Org. Chem.* 2000, 4:945-71) in further view of Zammetteo (*Analytical Biochemistry*; 2000) and Lukhtanov (WO 01/09385). The rejection is respectfully traversed for at least the reasons set forth below.

The law regarding obviousness is set forth in the above section. A feature of the pending claims "an array of at least two different polymer ligands [or nucleic acids] that differ by monomeric sequence covalently attached to different and known locations of a surface of a substrate ..."

Barner fails to teach or suggest this required element for the reasons set forth above. Therefore, Barner is deficient in teaching or suggesting all the claimed limitations.

As Beatie and Sanchez-Carbayo, were cited solely for their alleged disclosure of the use of cDNA in biosensors, neither reference remedies the deficiencies of Barner. Further, as Zammetteo and Lukhtanov were cited solely for their alleged disclosure of the use of aldehydes and benz aldehydes as ligand reactive functional groups for linking oligonucleotides to a solid support, they fail to cure the deficiencies of the primary reference.

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Because the references, either alone or when combined, fail to teach all the claim limitations, they cannot render the claimed invention obvious under 35 U.S.C. § 103(a). Accordingly, a *prima facie* case of obviousness has not been established and Applicants respectfully request that the rejection of claims 7-14, 16-23, 25, 26, 44, 48-51 be withdrawn.

Claims 7-14, 16-23, 25, 26, and 44-51 have been rejected under 35 U.S.C. § 103(a) as allegedly obvious over Barner et al. (EP 0596421 A1) in view of Beatie et al. (WO 95/11755) and Sanchez-Carbayo et al. (*Curr. Org. Chem.* 2000, 4:945-71) in further view of Achard et al. (*Bioinformatics Review* 2001). The rejection is respectfully traversed for at least the following reasons.

The law regarding obviousness is set forth in the sections above. A feature of the pending claims is "an array of at least two different polymer ligands [or nucleic acids] that differ by monomeric sequence covalently attached to different and known locations of a surface of a substrate ..."

Barner fails to teach or suggest this required element for the reasons set forth above. Therefore, Barner is deficient in teaching or suggesting all the claimed limitations.

As Beatie and Sanchez-Carbayo, were cited solely for their alleged disclosure of the use of cDNA in biosensors, neither reference remedies the deficiencies of Barner. Further, as Achard was cited solely for its alleged disclosure of the use of XML to remotely "forward" data to a "remote" location, it also fails to cure the deficiencies of the primary reference.

Because the references, either alone or when combined, fail to teach all the claim limitations, they cannot render the claimed invention obvious under 35 U.S.C. § 103(a). Accordingly, a *prima facie* case of obviousness has not been established and Applicants respectfully request that the rejection of claims 7-14,

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16-23, 25, 26, and 44-51 be withdrawn.

Claims 7-26, and 44-51 have been rejected under 35 U.S.C. § 103(a) as allegedly obvious over Barner et al. (EP 0596421 A1) in view of Beatie et al. (WO 95/11755) and Sanchez-Carbayo et al. (*Curr. Org. Chem.* 2000, 4:945-71), Zammetteo (*Analytical Biochemistry*, 2000), Lukhtanov (WO 01/09385), Bethell et al. (*J. of Chromatography*, 1981) and Orlowska (*Polish J. of Chem.*, 1980). The rejection is respectfully traversed for at least the following reasons.

The law regarding obviousness is set forth above. Again, a feature of the pending claims is "an array of at least two different polymer ligands [or nucleic acids] that differ by monomeric sequence covalently attached to different and known locations of a surface of a substrate"

Barner fails to teach or suggest this required element for the reasons set forth above. Therefore, Barner is deficient in teaching or suggesting all the claimed limitations.

As Beatie and Sanchez-Carbayo, were cited solely for their alleged disclosure of the use of cDNA in biosensors, neither reference remedies the deficiencies of Barner. Further, as Zammetteo and Lukhtanov were cited solely for their alleged disclosure of the use of aldehydes and benz aldehydes as ligand reactive functional groups for linking oligonucleotides to a solid support, they fail to cure the deficiencies of the primary reference. And, as Bethell and Orlowska were cited solely for their alleged disclosure of the use of imidazole carbamates, they do not supply the missing elements of Barner.

Because the references, either alone or when combined, fail to teach all the claim limitations, they cannot render the claimed invention obvious under 35 U.S.C. § 103(a). Accordingly, a *prima facie* case of obviousness has not been established and Applicants respectfully request that the rejection of claims 7-26,

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and 44-51 be withdrawn.

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In view of the amendments and remarks above, Applicants respectfully submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone Bret Field at (650) 327-3400.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-1078.

Respectfully submitted,

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